

## Experimental verification of TRiP-OER \*

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One of the key challenges for advanced radiotherapy is the possibility to adapt the treatment to patient-specific features, i.e. to perform an *adaptive treatment planning*. Among these features, increased radioresistance of tumor regions due to hypoxia (lower degree of cells' oxygenation) assumes a crucial importance, given the extremely poor prognosis connected with this phenomenon. Ion beam radiation allows in principle a larger flexibility and a higher potential for achieving an efficient adaptive treatment planning, but specific tools are lacking.

The TRiP98 code [1], pioneer treatment planning system for ion beams, which contributed to the success of the GSI pilot therapy project, was then recently extended toward this direction, and specifically, to implement the biological optimization including the hypoxia-induced radioresistance, i.e., the oxygen enhancement ratio (OER).

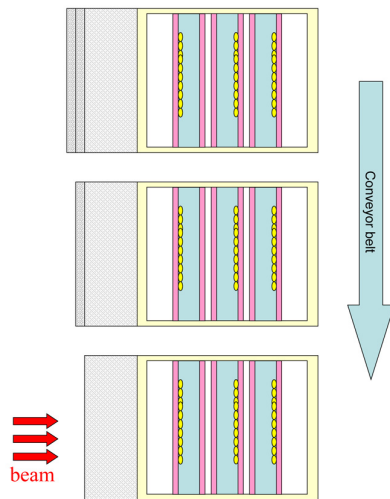


Figure 1: Experimental setup (see text).

The TRiP-OER extension mainly consist in the possibility to introduce a selective treatment of differently oxygenated areas of a tumor, once its spatial oxygenation map is provided as an input (e.g. exploiting the recent PET functional imaging techniques [2]), through an effect-based optimization aiming at restoring a prescribed survival level in the overall tumor. The extension relies on a semiempirical model description of the OER as a function of LET and oxygen concentration ( $pO_2$ ) [3], and the modification of the biological effect calculations introduced into the code

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and allowing to perform not only forward but also inverse planning, obtaining an effective OER driven optimization [4,5].

Dedicated experiments were then designed to verify the expected survival predicted by the code in a carbon ion extended target irradiation, and specifically, with a focus on the very last part of the extended volume, where the LET effect in suppressing the OER is maximum and has a steep gradient. This has been done by exposing CHO-K1 cells in the GSI patented hypoxic triple ring chambers [6] in a sequence designed to cover densely the relevant depth region (Fig.1): the chambers containing the rings filled with medium were exposed to the beam by a conveyor belt in anoxic and normoxic conditions.

The experiments, performed during several carbon beamtimes in 2011 and 2012, returned, despite a consistent experimental uncertainty, a remarkable agreement with the calculations of TRiP-OER (Figure 2).

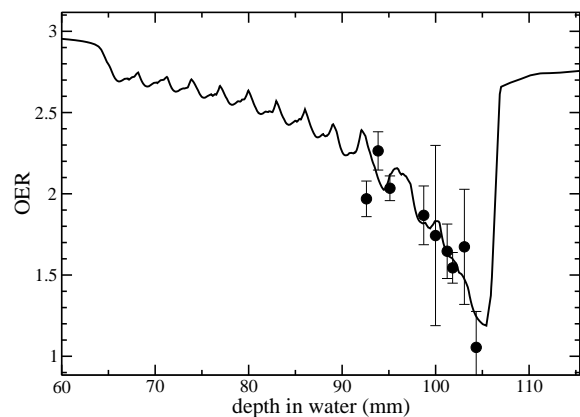


Figure 2: TRiP-OER computed OER values across a single field extended target irradiation (line) and corresponding experimental data (points).

## References

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